REMARKS

I. Formal Matters

The Examiner has not indicated whether the drawings filed on January 23, 2001 have been accepted.

The Examiner is requested respectfully to indicate that the drawings are acceptable.

The Examiner has not returned an initialed copy of Form PTO-1449 filed with the Information Disclosure Statement of January 23, 2001.

The Examiner is requested respectfully to return this form along with the next communication.

II. Detailed Action

A. Status of Claims

Claims 1, 3, 5, 6, 11, 12, 17, 19-22, 25 and 29-35 are pending. Claims 5, 7-10, 17, 19-22, 29 and 31-34 are withdrawn from consideration as being directed to a non-elected invention.

B. Claim Objection

In Paragraph No. 6 of the Office Action, claims 6 and 11 are objected to because of the term "to any of claims 1-4." The Examiner suggests the use of --to any one of claims 1-4--. The Examiner also makes a similar assertion regarding claim 35.

The Examiner's suggestion has been adopted. Therefore, the objection should be removed.

C. Rejections under 35 U.S.C. §112

1. In Paragraph No. 7 of the Office Action, claims 1-4, 6, 11 and 12 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not sufficiently described in the specification.

The Examiner asserts that claim 1 incorrectly recites the activity of galectin-3 rather than a compound that inhibits the activity of galectin-3.

Claim 1 has been amended to recite that the activity of the compound is inhibited.

2. In Paragraph No. 8 of the Office Action, claims 25-28, 30, 35 and 36 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification.

Essentially, the Examiner asserts (1) that the specification does not show that a compound that inhibits the overproduction and accumulation of extracellular matrix actually inhibits a specific disease, and (2) that there is no description of every specific compound that inhibits the overproduction and accumulation of extracellular matrix promoted by galectin-3.

For the following reasons, this rejection is traversed, respectfully.

Regarding the phrase "the inhibition of glomerular nephritis, diabetic nephropathy or tissue fibrosis" found in claim 25, it is well known in the art that an accumulation of extracellular matrix causes the diseases recited in the claims, such as glomerular nephritis, diabetic nephropathy, tissue fibrosis, and others. On the other had the present inventors newly found that galectin-3 promotes the accumulation of the extracellular matrix. Therefore, it is reasonable to expect that a substance that inhibits the activity of galectin-3, also inhibits glomerular nephritis, diabetic nephropathy and tissue fibrosis.

The relationship between the accumulation of extracellular matrix (ECM) and tissue fibrosis is described in the specification on page 2, lines 5 to 8, which reads "the overproduction and the accumulation of extracellular matrix (ECM) such as collagen is believed to be an important factor for the pathogenesis of the fibrosis of tissues." In addition, the specification, on page 2, lines 31 to 33, describes that the activated Ito cells proliferate and produce ECM in an excess amount in the Disse's space to thereby cause hepatic fibrosis.

Regarding glomerular nephritis and diabetic nephropathy, the specification, on page 3, lines 4 to 10, describes that "the activated mesangium cells proliferate while themselves also producing cytokines such as PDGF and TGF-β together within excessive amount of ECM, creating factors that cause various glomerular diseases, for example, chronic glomerular nephritis, including IgA nephropathy, diabetic nephropathy...."

Since ECM causes the claimed diseases, it is clear that a decrease in ECM alleviates the claimed diseases.

On the other hand, as can be seen from Examples 4 and 5, galectin-3 promotes the production and accumulation of type IV collagen, which represents the extracellular matrix.

Therefore, it is expected that a substance that inhibits the activity of galectin-3 also inhibits the promotion of the production and accumulation of extracellular matrix by galectin-3, resulting in inhibition or alleviation of the claimed diseases caused by the accumulation of extracellular matrix such as collagens.

The above-mentioned expectation is supported by some articles regarding "Pirfenidone" "PDF," which has been confirmed to inhibit the production and accumulation of collagen that is in extracellular matrix. Specifically, according to *Kidney International*, Vol. 52, Suppl. 63 (1997), pp. S-239-243 (copy submitted herewith), in the 5/6 nephrectomy rat model, PFD inhibited the overproduction of collagen IV, and alleviated chronic renal failure, proteinuria, *etc.* According to *Kidney International*, Vol. 54, (1998), pp. 99-109 (copy submitted herewith) in the unilateral ureteral obstruction model (UUO), PFD inhibited the overproduction of collagen, and alleviated renal diseases. According to *Biochemical Pharmacology*, Vol. 64 (2002), pp. 517-525 (copy submitted herewith), in the vanadate-induced kidney fibrosis model, PDF inhibited the

overproduction of hydroxyproline that is a marker for collagen production, and alleviated renal disorders.

Therefore, applicants submit, respectfully, that one of ordinary skill in the art as of the effective filing date of the present application, would expect that compounds that inhibit the overproduction and accumulation of extracellular matrix promoted by galectin-3 would be useful to treat diseases caused by such overproduction and accumulation of extracellular matrix.

If the Examiner desires, applicants will submit the above comments in the form of a Declaration under 37 C.F.R. § 1.132.

Regarding the scope of galectin-3 inhibitors, the Examiner's attention is directed to the specification, page 6, line 11 to page 8, line 10, wherein are listed numerous ways that the activity of galectin-3 can be inhibited. Substances that inhibit galectin-3 can be easily selected from candidate substances by a person with ordinary skill in the art by applying a conventional screening method for galectin-3. For example, galectin-3 inhibitors may be selected by the following steps:

(1) immobilizing a sugar ligand (such as fetuin, LNFP-1 *etc.*) to wells of a 96-well plate,

(2) adding a mixture of a substance to be tested and galectin-3 to the wells,

(3) detecting galectin-3 immobilized to the well via the sugar ligand by an anti-galectin-3 antibody, and

(4) determining whether or not the tested substance is a galectin-3 inhibitor on the basis of the amount of galectin immobilized to the wells.

Accordingly, one skilled in the art knows how to identify appropriate compounds useful in the claimed method.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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